

THE LANCET

Infectious Diseases

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed.
We post it as supplied by the authors.

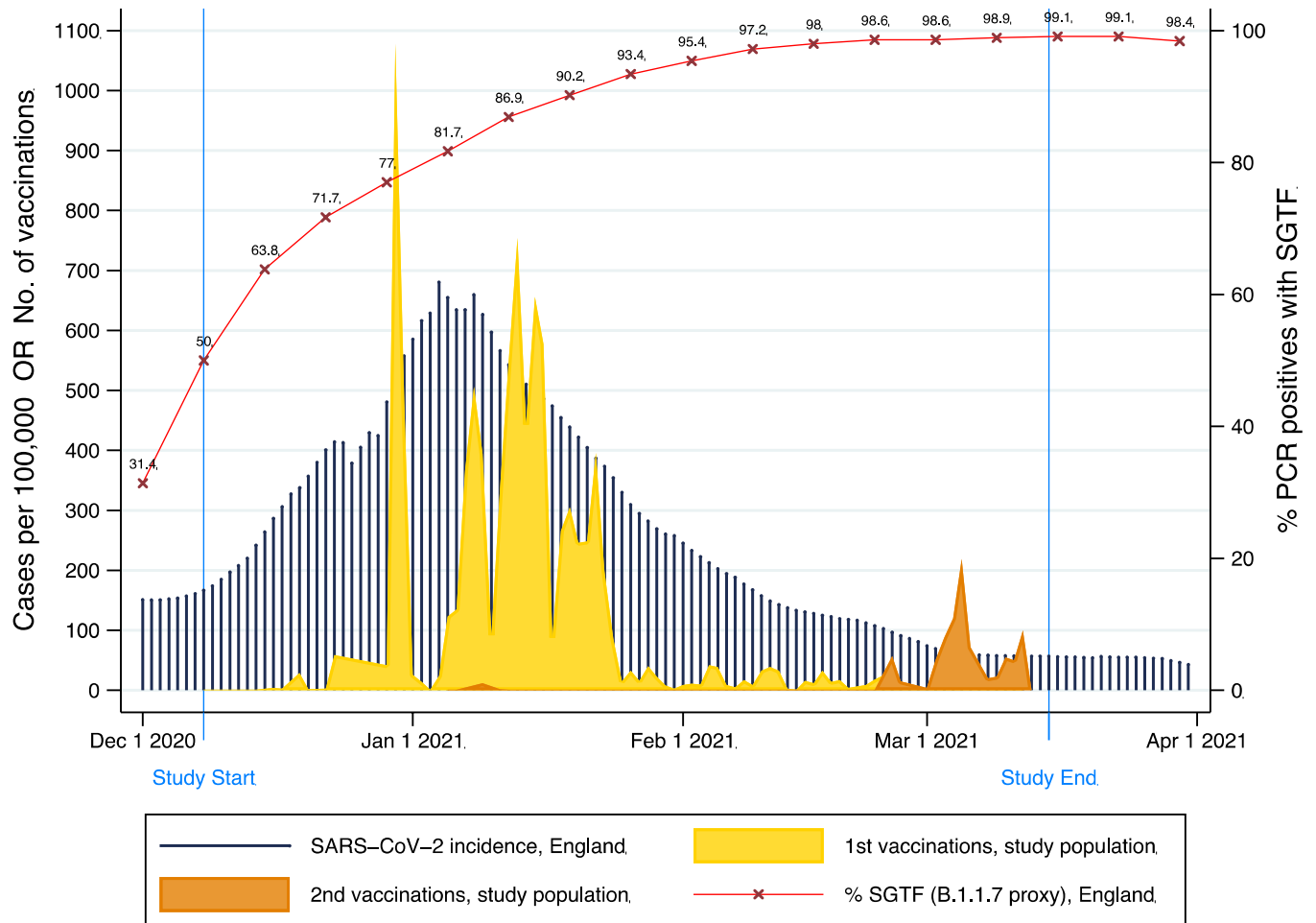
Supplement to: Shrotri M, Krutikov M, Palmer T, et al. Vaccine effectiveness of the first dose of ChAdOx1 nCoV-19 and BNT162b2 against SARS-CoV-2 infection in residents of long-term care facilities in England (VIVALDI): a prospective cohort study. *Lancet Infect Dis* 2021; published online June 23. [https://doi.org/10.1016/S1473-3099\(21\)00289-9](https://doi.org/10.1016/S1473-3099(21)00289-9).

Supplementary Materials

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I. Background epidemiology and study cohort vaccination over the study period

Figure S1 – Daily national SARS-CoV-2 incidence rates*, percentages of PCR positives with SGTF**, and numbers of study cohort vaccinations.



* Daily national incidence rates data for England are taken from a publicly available resource: <https://coronavirus.data.gov.uk>.

[Accessed 30 April 2021].

**SGTF – Spike gene target failure in the context of a positive PCR assay is used as a proxy for the presence of the B.1.1.7 variant of concern. SGTF occurs reproducibly on the Thermo Fisher TaqPath assay that is used in 3 UK laboratories that process Pillar 2 samples. Weekly SGTF data for England are taken from a publicly available resource:

<https://www.gov.uk/government/publications/investigation-of-novel-sars-cov-2-variant-variant-of-concern-20201201>. [Accessed 30 April 2021].

II. Additional Methods

The COVID-19 national testing programme was rapidly set up in response to the pandemic in April 2020 and consists of five testing Pillars [<https://www.gov.uk/government/publications/coronavirus-covid-19-scaling-up-testing-programmes>]. Samples from the VIVALDI study are processed under Pillar 1 or Pillar 2 of this programme. Testing for Pillar 1 is undertaken in hospital settings or as part of public health outbreak investigations and samples are processed in NHS hospitals. Pillar 2 encompasses surveillance testing in community settings such as LTCFs and schools. These samples are processed in a national network of accredited laboratories that use a range of PCR-based assays targeting up to three SARS-CoV-2 genes, including N, ORF, and S. The majority of PCR test results included in this analysis were from routine testing, therefore were processed through Pillar 2, and it was only possible to obtain Ct values for Pillar 2 samples.

Table S1. Details of laboratories, assay manufacturers, and gene targets for samples included in Ct values analysis (Pillar 2 only)

Laboratory	Assay Manufacturer	Gene target results available*	Gene target results used*
Newport Charnwood Immensa	PerkinElmer	N, ORF1ab	N, ORF1ab
Milton Keynes Glasgow Alderley Park Oncologia University of Birmingham	Thermo Fisher	N, ORF1ab, S	N, ORF1ab, S
Health Services Laboratories		N	N
Cambridge	Primer design	ORF1ab	ORF1ab
Randox	Randox	ORF1ab, E	ORF1ab
Accora Lab Zotz	BGI	ORF1ab	ORF1ab
iDNA	ID Solutions	N1, N2	N1, N2

*N/N1/N2 = nucleocapsid protein; ORF1ab = open reading frame 1ab polyprotein; S = spike protein; E = envelope protein

Serum samples were analysed to detect SARS-CoV-2 nucleocapsid IgG using the Abbott ARCHITECT system (Abbott, Maidenhead, UK). An index value of 1.4 is used to define a positive result, in line with manufacturer recommendations. Antibody test results were submitted to NHS England and matched to the NHS number using an

algorithm based on participant forename and surname, date of birth, sex and postcode to generate the common pseudo-identifier enabling linkage to PCR test results in the COVID-19 Datastore.

The legal basis for accessing personal data from staff and residents without consent under the General Data Protection Regulations (GDPR) was provided by the Coronavirus (COVID-19): notice under 3(4) of the Health Service (Control of Patient Information) Regulations 2002, which was issued by the UK Government to support the national response to COVID-19 [<https://www.gov.uk/government/publications/coronavirus-covid-19-notification-of-data-controllers-to-share-information/coronavirus-covid-19-notice-under-regulation-34-of-the-health-service-control-of-patient-information-regulations-2002-general—2>].

III. Secondary analysis: Cycle threshold values of PCR-positives

Table S2. Mean Ct values from all available PCR-positive results, by days since the first vaccine dose.

Vaccination status	Samples	Mean Ct value	Std. Deviation	95% CI		p-value
Unvaccinated	552	26.55	6.57	26.00	27.10	NA
0-27 days	411	25.91	7.38	25.19	26.62	0.1582
28+ days	107	31.29	8.71	29.62	32.96	<0.0001

NA – not applicable

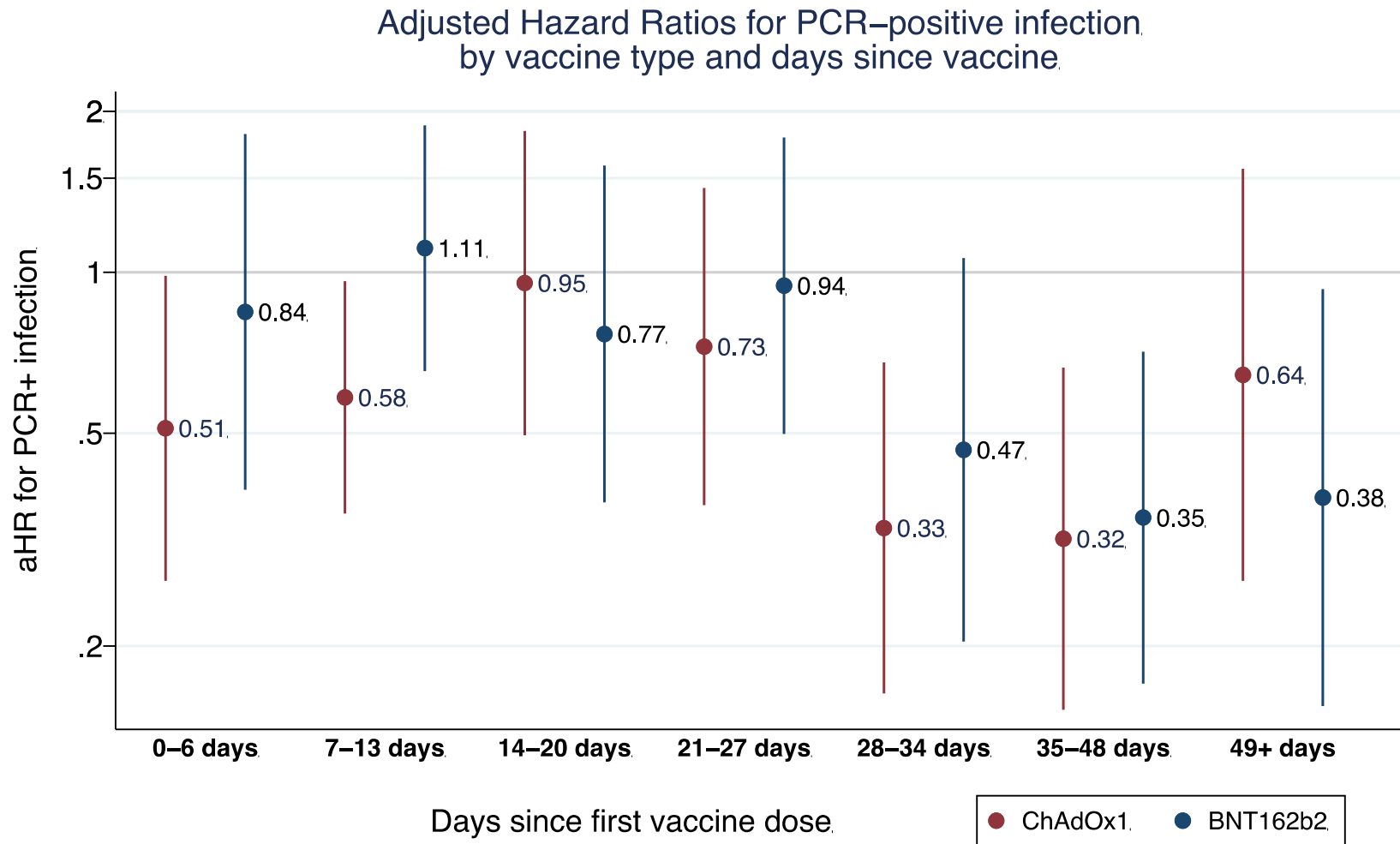
Table S3. Sensitivity analysis using mean Ct values of results from a single assay* only, by days since the first vaccine dose.

Vaccination status	Samples	Mean Ct value	Std. Deviation	95% CI		p-value
Unvaccinated	246	28.70	5.92	27.96	29.45	NA
0-27 days	146	28.84	7.26	27.66	30.03	0.8369
28+ days	71	34.75	7.37	33.01	36.50	<0.0001

NA – not applicable

*The single assay for which the greatest total number of results were available was the PerkinElmer SARS-CoV-2 Real-time RT-PCR Assay, used by Newport, Charnwood, and Immensa labs (Table S1). Results from other assays were excluded for this sensitivity analysis.

IV. **Figure S2.** Secondary Analysis - Adjusted hazard ratios (aHR)* for PCR-positive infection by vaccine type and days since vaccination



*Adjusted hazard ratios for infection estimated using Cox proportional regression model and presented with 95% confidence intervals. Hazard ratios are relative to the unvaccinated group, and adjusted for age, sex, prior infection (positive PCR or antibody result) LTCF bed capacity, and local infection incidence rates. 95% confidence intervals are calculated using robust standard errors.

V. Secondary analysis – vaccine effect against infection by prior infection status

Table S4. Adjusted hazard ratios for PCR-confirmed infection by days since vaccination, in the group with no evidence of prior infection*, overall and stratified by vaccine type.

Days since first vaccine dose	No evidence of prior infection														
	OVERALL							ChAdOx1				BNT162b2			
	Person days at risk	Infection events	Infection rate per 10,000 person days	aHR	aHR 95% CI		p-value	aHR	aHR 95% CI		p-value	aHR	aHR 95% CI		p-value
Unvaccinated	297,832	711	23·87	1	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
0-6 days	41,548	104	25·03	0·64	0·39	1·07	0·090	0·51	0·26	0·99	0·047	0·86	0·40	1·86	0·706
7-13 days	46,684	134	28·70	0·82	0·54	1·26	0·362	0·57	0·35	0·93	0·023	1·10	0·65	1·88	0·720
14-20 days	43,799	122	27·85	0·90	0·54	1·52	0·701	0·93	0·48	1·78	0·822	0·69	0·33	1·43	0·320
21-27 days	41,229	94	22·80	0·93	0·54	1·61	0·791	0·72	0·36	1·44	0·358	0·97	0·51	1·83	0·923
28-34 days	37,260	42	11·27	0·45	0·24	0·83	0·010	0·34	0·17	0·69	0·003	0·48	0·21	1·09	0·078
35-48 days	54,554	54	9·90	0·36	0·18	0·73	0·005	0·30	0·14	0·64	0·002	0·33	0·16	0·67	0·002
49+ days	23,772	39	16·41	0·49	0·20	1·17	0·108	0·61	0·24	1·54	0·298	0·39	0·16	0·95	0·038
Total	586,678	1,300	22·16	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

NA – not applicable

Adjusted hazard ratios were estimated using a Cox proportional hazards regression model with an interaction term between vaccination status and prior infection status; the comparator is the unvaccinated group with no evidence of prior infection. Hazard ratios are adjusted for age, sex, local monthly infection incidence, LTCF bed capacity, and for estimates from the group with evidence of prior infection (results not displayed); 95% confidence intervals are calculated using robust standard errors for LTCF-level effects. In unvaccinated individuals with evidence of prior infection, when compared with the unvaccinated group without prior infection, the aHR for infection was 0.12 (0.04, 0.35).

*Prior infection was defined by a positive PCR result prior to 8 December 2020 or a positive antibody test prior to vaccination was considered evidence of prior infection.

Table S5. Adjusted hazard ratios for PCR-confirmed infection by days since vaccination, in the group with evidence of prior infection* (results not stratified by vaccine type due to small numbers).

Days since first vaccine dose	Evidence of prior infection						
	OVERALL						
	Person days at risk	Infection events	Infection rate per 10,000 person days	Adjusted Hazard Ratio	aHR 95% CI		p-value
Unvaccinated	40,171	12	2·99	1	NA	NA	NA
0-6 days	6,043	1	1·65	0·33	0·03	3·22	0·339
7-13 days	6,827	5	7·32	1·63	0·32	8·36	0·560
14-20 days	6,563	10	15·24	3·82	0·90	16·32	0·070
21-27 days	6,285	1	1·59	0·51	0·05	5·02	0·561
28-34 days	5,876	0	0	0	NA	NA	NA
35-48 days	8,458	5	5·91	1·66	0·39	7·15	0·493
49+ days	3,727	1	2·68	0·69	0·07	7·08	0·751
Total	83,950	35	4·17	NA	NA	NA	NA

NA – not applicable

Adjusted hazard ratios were estimated using a Cox proportional hazards regression model with an interaction term between vaccination status and prior infection status; the comparator is the unvaccinated group with evidence of prior infection. Hazard ratios are adjusted for age, sex, local monthly infection incidence, LTCF bed capacity, and for estimates from the group with evidence of prior infection. 95% confidence intervals were calculated using robust standard errors for LTCF-level effects.

*Prior infection was defined by a positive PCR result prior to 8 December 2020 or a positive antibody test prior to vaccination was considered evidence of prior infection.

VI. Sensitivity analysis - VE against infection excluding never vaccinated sub-group

Table S6. Characteristics of the never-vaccinated residents, and of the sub-group of never vaccinated residents excluded from the denominator for the sensitivity analysis.

Never vaccinated residents	<i>n</i>	%
Total	1,252	12·0%
Age (years)	Median: 86	IQR: 80-92
Female sex	810	65·0%
Prior infection	84	6·7%
LTCFs	271	87·4%
PCR positives in analysis period	328	26·2%
- Routine PCR testing	251	76·5%
- Symptomatic at time of routine testing	20	8·0%
Total never vaccinated with 1+ PCR test >30 days after LTCF first vaccination	439	35·1%
Age (years)	85	IQR: 79-91
Female sex	284	64·7%
Prior infection	37	8·4%
LTCFs	165	53·2%
PCR positives in analysis period	23	5·2%
- Routine PCR testing	20	87·0%
- Symptomatic at time of routine testing	1	5·0%

VII. **Table S7.** Sensitivity analysis: adjusted hazard ratios for PCR-positive infection by days since vaccination, excluding never vaccinated individuals who continued to be PCR tested*, overall and by vaccine type.

Days since first vaccine dose	OVERALL							ChAdOx1				BNT162b2			
	Person days at risk	Infection events	Infection rate per 10,000 person days	aHR	aHR 95% CI		p-value	aHR	aHR 95% CI		p-value	aHR	aHR 95% CI		p-value
Unvaccinated	308,217	700	22.7	1	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
0-6 days	47,591	105	22.1	0.54	0.32	0.92	0.024	0.40	0.20	0.79	0.008	0.78	0.36	1.66	0.513
7-13 days	53,511	139	26.0	0.67	0.41	1.09	0.105	0.40	0.23	0.68	0.001	0.96	0.57	1.63	0.881
14-20 days	50,362	132	26.2	0.72	0.41	1.28	0.266	0.56	0.27	1.14	0.110	0.59	0.29	1.23	0.159
21-27 days	47,514	95	20.0	0.64	0.34	1.24	0.187	0.37	0.18	0.77	0.008	0.63	0.32	1.24	0.180
28-34 days	43,136	42	9.7	0.29	0.13	0.63	0.002	0.15	0.07	0.36	<0.001	0.27	0.11	0.64	0.003
35-48 days	63,012	59	9.4	0.24	0.09	0.63	0.004	0.14	0.05	0.37	<0.001	0.17	0.07	0.41	<0.001
49+ days	27,499	40	14.6	0.31	0.09	1.03	0.057	0.29	0.09	0.97	0.044	0.17	0.05	0.55	0.003
Overall	640,842	1,312	20.5	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

NA – not applicable

Adjusted hazard ratios were estimated using Cox proportional hazards regression according to days since the first vaccine dose. Hazard ratios are adjusted for age, sex, local monthly infection incidence, LTCF bed capacity, and for estimates from the group with evidence of prior infection. 95% confidence intervals were calculated using robust standard errors for LTCF-level effects.

*Excluding individuals who remained unvaccinated despite PCR test results from more than 30 days after vaccination commenced at their LTCF.

STROBE Statement

	Item No	Recommendation	Page No
Title and abstract			
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5,6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5,6
Participants	6	a) Cohort study? Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-7
		(b) Cohort study? For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7

<i>Bias</i>	9	<i>Describe any efforts to address potential sources of bias</i>	7
<i>Study size</i>	10	<i>Explain how the study size was arrived at</i>	7
<i>Quantitative variables</i>	11	<i>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why</i>	7
<i>Statistical methods</i>	12	<i>(a) Describe all statistical methods, including those used to control for confounding</i>	7
		<i>(b) Describe any methods used to examine subgroups and interactions</i>	7
		<i>(c) Explain how missing data were addressed</i>	5-7
		<i>(d) Cohort study. If applicable, explain how loss to follow-up was addressed</i>	6,7
		<i>(e) Describe any sensitivity analyses</i>	6
Results			
<i>Participants</i>	13*	<i>(a) Report numbers of individuals at each stage of study? eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</i>	7, Fig. S1
		<i>(b) Give reasons for non-participation at each stage</i>	Fig. S1
		<i>(c) Consider use of a flow diagram</i>	Fig. S1
<i>Descriptive data</i>	14*	<i>(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders</i>	7, Tables 1,2
		<i>(b) Indicate number of participants with missing data for each variable of interest</i>	7, Table 1, Fig. S1
		<i>(c) Cohort study? Summarise follow-up time (eg average and total amount)</i>	8, Table 3

<i>Outcome data</i>	<i>15*</i>	<i>Cohort study? Report numbers of outcome events or summary measures over time</i>	<i>8, Table 3</i>
<i>Main results</i>	<i>16</i>	<i>(a) Report the numbers of individuals at each stage of the study? eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</i>	<i>7, Fig. S1</i>
		<i>(b) Give reasons for non-participation at each stage</i>	<i>Fig. S1</i>
		<i>(c) Consider use of a flow diagram</i>	<i>Fig. S1</i>
<i>Other analyses</i>	<i>17</i>	<i>Report other analyses done? eg analyses of subgroups and interactions, and sensitivity analyses</i>	<i>8,9, Tables 3,4, Tables S2-7</i>
<i>Discussion</i>			
<i>Key results</i>	<i>18</i>	<i>Summarise key results with reference to study objectives</i>	<i>9</i>
<i>Limitations</i>	<i>19</i>	<i>Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.</i>	<i>10</i>
<i>Interpretation</i>	<i>20</i>	<i>Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence</i>	<i>3,9,11</i>
<i>Generalisability</i>	<i>21</i>	<i>Discuss the generalisability (external validity) of the study results</i>	<i>9,10</i>
<i>Other information</i>			
<i>Funding</i>	<i>22</i>	<i>Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based</i>	<i>2,7</i>

